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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/464,377	12/15/99	STALLCUP	M 13761-726

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EXAMINER	
PROUTY, R	
ART UNIT	PAPER NUMBER
1652	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/464,377	Applicant(s) Stallcup t al.
	Examiner R becca Pr uty	Art Unit 1652

-- Th MAILING DATE of this communication appears n th cover sheet with the c rrespond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Mar 28, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-38 is/are pending in the applica

4a) Of the above, claim(s) 4-38 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-3 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Applicant's election with traverse of Group I, Claims 1-3 in Paper No. 12 is acknowledged. However, as previously presented the reasons for restriction contained several typographical errors which made them confusing at best. As such the restriction requirement in its entirety is repeated herein and will not be made final in this action in order to give applicants a chance to traverse the restriction as it was intended to be presented.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, drawn to DNA, vectors and host cells encoding a protein arginine methyltransferase, classified in class 435, subclass 325.

II. Claims 4-13, drawn to a protein arginine methyltransferase, classified in class 435, subclass 193.

III. Claims 14-16, drawn to antibodies to protein arginine methyltransferase, classified in class 530, subclass 387.9.

IV. Claims 17-20, drawn to methods of methylating a polypeptide, classified in class 435, subclass 68.1.

V. Claim 21, drawn to methylated histone H3, classified in class 530, subclass 358.

VI. Claim 22, drawn to antibodies to methylated histone H3, classified in class 530, subclass 389.1.

VII. Claims 23-26, drawn to assays for modulators of CARM1/GRIP-1 binding, classified in class 435, subclass 7.1.

VIII. Claims 27-32, drawn to methods of modulating expression of a nuclear-receptor dependent gene, classified in class 435, subclass 375.

IX. Claims 34-38, drawn to methods of screening for modulators of CARM1 coactivator activity, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

The DNA of Group I, and the proteins of Groups II, III, V and VI, each comprise a chemically unrelated structure capable of separate manufacture, use and effect. The DNA comprises a nucleic acid sequence, and the proteins of Groups II, III, V and VI each comprise unrelated amino acid sequences. The DNA has other utility besides encoding the proteins such as a hybridization probe, the proteins can be made by another method such as isolation from natural sources or chemical synthesis and the proteins have other utility besides acting as an antigen to induce the antibodies such as for the methods of Group IV.

Inventions II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product can be used to induce antibodies.

Inventions IV and V are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product can be made by a materially different method such as chemical synthesis.

The DNA of Group I, the antibody of Group III, and the antibody of Group VI are unrelated to the method of Group IV as they are neither used nor made by the method of Group IV.

Inventions I and VII, VIII or IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another

materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the DNA of Group I can be used to produce the proteins of Group II.

The proteins of Group II, the antibody of Group III, the histones of Group V and the antibody of Group VI are unrelated to the methods of Group VII-IX as they are neither used nor made by the methods of Group VII-IX.

The methods of Groups IV and VII-IX are independent as they comprise different steps, utilize different products and produce different results.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter as shown by their different classification, restriction for examination purposes as indicated is proper.

Claims 4-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (upon which Claims 2-3 depend) is indefinite in the recitation of "substantially equivalent". This phrase is defined on page 14 of the specification as "a sequence which varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences". However, this definition is unclear as it does not specify what functions are referred to nor define what would constitute an "adverse functional dissimilarity". The sequence of SEQ ID NO:1 encodes a protein with several different functions, including protein-arginine methyltransferase activity and as a coactivator of transcription. Must all of the functions of the reference sequence be maintained? or only some or one?

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules comprising a sequence substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides. The specification

does not contain any disclosure of the function of all DNA sequences that are substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides. The genus of nucleic acids encompassed is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for any nucleic acid comprising a sequence substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3 are so broad as to encompass any nucleic acid comprising a sequence substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single gene encoding a protein-arginine methyltransferase and the encoded amino acid sequence.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and

the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any nucleic acid comprising a sequence substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting protein-arginine methyltransferase activity; (B) the general tolerance of protein-arginine methyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any protein-arginine methyltransferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any nucleic acid comprising a sequence substantially equivalent to SEQ ID NO:1 or a fragment thereof of at least 40 nucleotides. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of

section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Chen et al.

Chen et al. teach the cloning and expression of a CARM1 nucleic acid identical to SEQ ID NO:1.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Lal et al.

Lal et al. teach a human nucleic acid (SEQ ID NO:6) which is 83% identical to nucleotides 290-2567 of SEQ ID NO:1 and including many stretches of 100% identity of greater than 40 nucleotides in length and vectors and host cells comprising this nucleic acid. This nucleic acid encodes a protein-arginine methyltransferase with 99% identity to amino acids 163-608 of SEQ ID NO:2.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank entries AA396116 and AA215095.

GenBank entry AA396116 teaches a nucleic acid which is 100% identical to nucleotides 2102-2678 of SEQ ID NO:1 and vectors and host cells comprising this nucleic acid.

GenBank entry AA215095 teaches a nucleic acid which is 99.5% identical to nucleotides 2154-2720 of SEQ ID NO:1 and including

many stretches of 100% identity of greater than 40 nucleotides in length and vectors and host cells comprising this nucleic acid.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652